

## **Comment for BSC meeting on Feb 24, 2009**

**Re:** Draft substance profile on aristolochic acids

**Submitted by:**

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The excellent draft profile should include an unequivocal statement of the well-documented risk that aristolochic acids pose to global human health when *Aristolochia* is used in traditional herbal remedies. The literature supporting this proposal can be found in the September 2 Background Report on Carcinogens but the conclusion I have drawn would be obscure to most readers. A clear warning does appear in recent reviews (1 and 2) that do not appear in the draft profile or Background Report.

My proposal is to add a short paragraph to the final report(s), based on published information cited in the Background Report, based on the following logic:

- Eighty percent of the world's population presently rely on herbal remedies to treat symptoms of disease.
- *Aristolochia* herbals have been used for centuries throughout Europe, Asia, Africa and North and South America. Remarkably, the extensive *materia medica* describing the medicinal use of *Aristolochia* never mentions their intrinsic toxicity.
- The governments of China and India, countries with populations in excess of one billion, have been slow to implement measures to reduce human exposure to this nephrotoxic and carcinogenic herb. For example, *Aristolochia* species are listed in official pharmacopias, tens of thousands of pounds of these species are harvested annually in China for medicinal purposes and significant amounts of this herb are exported (legally and illegally) to other countries including the United States.
- The upper urothelial cancer associated with aristolochic acid nephropathy exists throughout the world as a "silent" but omnipresent iatrogenic disease. This cancer, initiated by exposure to aristolochic acids, develops in 50% or more of individuals exposed over time to low doses of aristolochic acid and often appears in the absence of overt renal disease.
- The remarkable persistence of AL-DNA adducts is such that even if aristolochic acid exposure ceased completely today, upper urothelial cell cancer would remain a public health problem for many years in the future.

- Aristolochic acid nephropathy is asymptomatic and there is no practical method of screening persons for exposure to this human carcinogen. By highlighting the carcinogenic potential of Aristolochia herbals in the 12<sup>th</sup> Report on Carcinogens, public health authorities responsible for the large populations at risk might be persuaded to take appropriate actions.

In summary, I posit that AAN and its associated upper urothelial cancer represents a long-overlooked iatrogenic disease and an international public health problem of considerable magnitude and propose that the NTP highlight this important warning in their final report.

1. F. D. DeBelle, J-L. Vanherweghem and J.L. Nortier, Aristolochic acid nephropathy: a worldwide problem. *Kidney Int.*, 2008 74: 158-169.
2. A. P Grollman, J. Scarborough and B. Jelaković. Aristolochic acid nephropathy: an environmental and iatrogenic disease. *Adv. Mol. Toxicol.* v3. J. Fishbein ed. Elsevier Press, New York, 2009, pp 217-233.